

The Prudent Prescriber

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Pharm Reps ≠ Rational Prescribing

(PR)



(RP)

Do Treatments for Dementia Improve Symptoms or Delay Progression?

Over the years, I have prescribed Aricept in spite of knowledge that this class of drugs is probably not very effective. Raina et al. study "Effectiveness of cholinesterase inhibitors and memantine for treating dementia" *Ann Int Med* 2008; 148:379 gives us the most definitive look yet at the value of these drugs.

- **Study design:** Meta-analysis (randomized controlled trials).
- **Data synthesis:** 96 publications with 59 unique randomized controlled trials that evaluated pharmacological agents for patients with a diagnosis of dementia. Studies were limited to those of good quality (Jahad score of 3 or better).
- **Evaluated:** Evidence for effectiveness of 5 drugs in improving outcomes in: cognition, global function, behavior and quality of life (including ADLs and caregiver burden).
- **Funding:** AHRQ and the Ontario Ministry of Health and Long Term Care.
- **Methods:** Two researchers independently abstracted data and assessed study quality. They classified a **clinically relevant** benefit as a difference in score of 4 or more points on the 70 point Alzheimer's Disease Assessment Scale (ADAS), the tool used most commonly for cognitive evaluation. These criteria apply to mild or moderate, but not severe dementia.
- **Results:**
 - 1) Only three studies (no surprise!) directly compared different cholinesterase inhibitors and found no outcome differences in cognition and behavior.
 - 2) The positive effect sizes were greatest in Alzheimer's dementia, next largest in those with vascular dementia and smallest in those with mild cognitive impairment.
 - 3) Most common reported adverse effects (AE) of the cholinesterase inhibitors were diarrhea (RR 2.57), nausea (RR 2.54) and anorexia (RR 3.21). AE were dose related.
 - 4) Elevated liver function studies were reported in 7-67% of the tacrine treated patients vs 4-13% in the placebo group.

**Antibiotics do
NOT**



**help
acute bronchitis**

**β-blockers in
post-MI
save
lives**

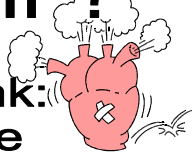


**Pill splitters save
big**



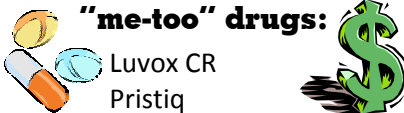
CHF?

Think:



**Ace
Aldactone
B-blocker
Dig
Diuretic**

**Avoid these expensive
"me-too" drugs:**



Luvox CR
Pristiq
Omnaris
Soma 250
AMrix XR
Xyzal
Veramyst
Ambien CR

**Treat diabetics
BP to 130/80**



Continued...



now available
on the
Generic Marquee

Razadyne → galantamine
Sonata → zaleplon
Fosamax → alendronate
Norvasc → amlodipine
Ambien → zolpidem
Flonase → fluticasone nasal

Treatments for Dementia, continued

5) When compared with placebo, each of the four cholinesterase inhibitors and memantine *produced a consistent, statistical improvement* in:

cognition behavior quality of life

but there were**No clinically significant effects!!**

The changes in the ADAS scores were consistently <4.

My Take:

- This study highlights the very critical difference between outcomes that are **statistically, but not clinically important**. In the words of the authors, the effects of these drugs are “**unimportant**.”
- This study provides an excellent evidence base for us to help demented patients and their families make prudent decisions regarding these highly marketed products.
- If you are pressured to prescribe one of the drugs, think short term re-evaluation! A majority of the studies lasted only 12 to 16 weeks and almost all were less than six months in duration.
- Avoid Tacrine (Cognex): poorest efficacy data and potential for liver toxicity.
- Costs: Aricept 5 mg or 10 mg/day for one month = \$170 (\$5.67/ day)
Namenda 10 mg BID for one month = \$156 (\$5.20/day)
Generic Razadyne (galantamine), just released = \$80/month

Pharmaceutical Outrage of the Month

- Deston Therapeutics, who makes Auralgan, has changed the formulation of their product by adding acetic acid (antibacterial, antifungal) and U-polycosan-101 (astringent) to the older product's ingredients of antipyrine and benzocaine.
- The original product was never approved by the FDA, but was “grandfathered in”. The “new” product also has not been approved by the FDA, but the manufacturer is sending faxes to pharmacies warning them not to substitute Auralgan prescriptions with the “old” antipyrine/benzocaine formulation.
- **Why does it matter?**
 - The old Auralgan costs pharmacies ~ \$2 / 10cc bottle**
 - The new Auralgan costs pharmacies ~ \$140 / 10cc bottle**
 - ? What's a doc to do?
 - The Prescriber's Letter suggests writing for A/B otic (antipyrine/benzocaine) \$10 or giving pharmacists permission to substitute.

Guidelines from the NICE People to Make Care Simpler ...and More Evidence Based?

- The British National Institute of Clinical Effectiveness (NICE) guidelines are derived from systematic reviews supplemented, when minimal evidence is available, with recommendations based on expert opinion.
- In making decisions about lipid lowering treatment, their basic premise is that it's the baseline risk not the baseline lipid levels that are of primary importance.

Their 2008 recommendations:

- ☼ For patients with elevated lipids, but without heart disease, the guidelines suggest no treatment if patients are at a 10 year risk of <20%.
- ☼ For those needing primary prevention (10 year risk >20%), they suggest a hands-off approach of treating with simvastatin 40 mg a day and **not checking a follow-up cholesterol**. (*I know this is anathema*)
- ☼ For patients with heart disease, they suggest starting with the same 40 mg of simvastatin, but checking the lipid response and increasing the dose until the total cholesterol is <155 mg per deciliter or the LDL is <77 mg per deciliter.

My Take:

- ☺ The NICE guidelines are certainly simpler and easier to interpret and implement than the convoluted ATP III. This approach makes sense, particularly given that most of our patients would not qualify for the studies that have been conducted on cholesterol lowering drugs.
- ☺ Compared to ATP III, NICE would recommend cholesterol lowering drugs much less frequently.
- ☺ How can two groups of scientists look at the world's literature and present us with such different approaches to cholesterol management?
- ☺ Why is there a sizable Merck/Schering-Plough advertisement on the American Heart Association website?
- ☺ An interactive model of the Framingham Risk calculator is available at <http://hp2010.nhlbi.nih.gov/atp3/calculator.asp?usertype=prof>

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